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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/587,653	06/05/2000	David V. Sangar	UTSG.231US	8912

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 08/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/587,653	SANGAR ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-21,29-33 and 51-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21,30-33 and 51-72* is/are rejected.

7)☒ Claim(s) *29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *July 11, 2006* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment and argument

This is a response to the amendment filed on 03/28/2006. Claim 19 has been amended. New claims 58-72 have been added. Claims 1-18, 22-28 and 34-50 were canceled. Claims 19-21, 29-33 and 51-72 are pending and considered before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

It is noted that applicants have submitted an amendment of the specification; however, the amendment of the specification does not compliant to the rule 37 CFR 1.121 because it does not list in which page of specification has been amended. The amended part of the specification needs to be marked too. Please resubmit the amendment with indication where the amendment should be placed and mark the change of the amended specification.

Priority

1. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. [1] as follows:

2. The later-filed application must be an application for a patent for an invention, which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

3. The claimed benefit of an earlier priority date of claims 51-55 based on the provisional application No. 60, 137,665, June 04, 1999 is still denied.

4. In response, applicants argue that the provisional application provides an ennoblement disclosure of claims 51-55 in page 4, page 9 and page 32 since applicants isolate the genome of the GBV-B that contains the claimed SEQ ID NO: 1, accordingly Applicants assert that one of an ordinary skilled in the art would be in possession of SEQ ID NO: 2, because the SEQ ID NO:

2 is the combined sequence of Genbank accession number U22304 and the 3' nucleotide sequence of GBV-B (SEQ ID NO: 1). Therefore, claims 51-55 are entitled to the priority date of June 04, 1999.

5. The disclosure of the specification in the provisional application No. 60, 137,665 has been carefully reviewed, especially the part that applicants pointed out having the enablement disclosure of the claimed SEQ ID NO: 2. It has been noted that the specification of "665" teaches that a new 3' non-coding sequence of SEQ ID NO: 3 identified from a genome of a GBV-B virus. However, although the precise sequence structure of SEQ ID NO: 1 has been described and disclosed under the first paragraph of 35 U.S.C. 112. the precise whole sequence of said GBV-B virus genome was not disclosed under first paragraph of 35 U.S.C. 112.

6. To the contrary of applicants' statement that SEQ ID NO: 2 is the combined sequence of Genbank accession number U22304 and the 3' nucleotide sequence of GBV-B (SEQ ID NO: 1, the disclosure of the page 32 states that the said isolated GBV-B viral genome is different from the published GBV-B virus genome of genebank accession number U22304. Because applicants were found to contain altered 14 amino acids that are different from the published sequence (U22304) and presumably 2 of them are definitely different from the published sequence. Although applicants listed all 14 possible altered amino acids that none of them located in the 3' non-coding sequence of SEQ ID NO: 1, the specification of the provision application "665" does not teach which 2 of the 14 are the remaining mutations.

7. Nevertheless, the precise sequence structure of the isolated GBV-B cloned is not disclosed under 112 1st paragraph. A person skilled in the art still does not know what the exact sequence structure of the isolated GBV-B virus genome is at the time of the provision application No. 60, 137,665 was filed on June 04, 1999.

8. Therefore, the benefit of the earlier filing date of claims 51-55 cannot be granted.

New ground objection and rejections:

Claim Objections

9. Claim 29 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

claim(s) in independent form. In the instant case, claim 29 is improper because it depends on the canceled claim 28. Therefore, it fails to define the subject matter in the claim, and it also cannot further limit the previous claimed subject matter because the previous claim is no longer existed. This objected is anticipated by the amendment filed on current amendment.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. In the instant case, claim 28 is vague and indefinite because it fails to define what the claimed subject is and it also fails to further limit the previous claimed subject. Because the previous claim is no longer existed.

Claim Rejections - 35 USC § 112

13. Claims 19-20, 30-33, 51-56 are still rejected under 35 U.S.C. 112, first paragraph under the same ground stated in the previous office action.

14. Applicants' argument has been respectfully considered; however it is not found persuasive to withdrawn the rejection and it is moot in view of the new ground rejection necessitated be applicants' amendment set forth below.

15. Claims 19-21, 30-33, 51-56 and 57-72 are rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for producing an infectious GBV-B virus or a chimeric GBV-B/HCV virus by providing the host liver cell of Tamarin with a full length of the GBV-B viral genome or BGV-B/HCV chimeric viral replicon in either a cDAN or a transcribe of said cDAN of SEQ ID NO: 2, which contains the full length of 3' terminal sequence of SEQ ID NO: 1, does not provide enablement for any person skilled in the art to have a method to produce any or all virus by providing any host cell with a recombinant GBV-B or chimeric GBV-B virus

genome comprising as long as a full length 3' terminal sequence, SEQ ID NO: 1 or a at least 50-100 contiguous nucleotide of SEQ ID NO: 1 presence or at least 70 to 95% of SEQ ID NO: 1 plus as long as 250 to 5000 contiguous nucleotides of SEQ ID NO: 2 presence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

16. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosure in the application coupled with information known in the art would render undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include, but are not limited:

17. A). The nature of the invention; B). The breadth of the claims; C). The state of art; D). The predictability of the art; E). The level of one of ordinary skilled in the art; F). The amount of direction provided by the inventor; G). The existence of working example.

18. In the instant case, the nature of the invention is a method for producing a recombinant GBV-B virus or the chimeric GBV-B/HCV virus by introducing a full length recombinant GBV-B virus RNA genome or a GBV-B/HCV chimeric virus replicon comprising either the full length of GBV-B virus of SEQ ID NO: 2 or partial GBV-B virus genome that comprise the full length of the 3' non-coding region of SEQ ID NO: 1 into the liver cells of a Tamarin. However, after amendment, the broad scope of the claims read a method for producing any virus by providing any host cell in vitro or in vivo a recombinant BGV-B or chimeric GBV-B genome as long as it comprises the 3' terminal sequence of SEQ ID NO: 1 or SEQ ID NO: 2 or even a contiguous 50 to 100 contiguous nucleotide of SEQ ID NO: 1 or 70% to 95% of SEQ ID NO: 1 along or partial contiguous nucleotide sequence of GBV-B cDAN of SEQ ID NO: 2 (250-5000).

19. The state of art teaches that virus is defined as "Any of a large group of submicroscopic agents that act as parasites and consist of a segment of DNA or RNA surrounded by a coat of protein. Because viruses are unable to replicate without a host cell, they are not considered living organisms in conventional taxonomic systems. Nonetheless, they are described as "live" when they are capable of replicating and causing disease." (See The Free Dictionary by FARLEX on

line, Google searches on August 11, 2006, pages 1-2) Therefore, a virus per se cannot be produce by only a portion or even the 3' non-coding region of any virus or portion of piece of DNA along. That is to say, an intact virus can be produced by a replicon that is able to express the virus coding and non-coding regions of genome, wherein the replicon is defined as a genetic element (e.g. a plasmid, chromosome, or virus) that functions as an autonomous unit of DNA replication in vivo or inside of host cell; i.e. is capable of replication under its own control (See lines 26-29 in column 7 of US Patent No. 5,672,350A). Moreover, providing that some appropriate viral early proteins are available for processing in a partial sequence or full length entire sequence of SEQ ID NO: 1 or SEQ ID NO: 2. However, these sequences are only required for the replication of a flavivirus, it cannot replicate to produce other virus that does not use same replication machinery like a flavivirus. The specification does not teach or provide sufficient guidance to support the broadly claimed scope of the invention.

20. While in the response, applicants argue that previous office action has improperly interpreted the present claims. Applicants content that the present claims are not directed to the methods of producing any virus in any host cell because the claim 19 reads "introducing into a host cell a recombinant GBV-B or chimeric GBV-B virus genome." However, the claims as drafted are directed to produce a virus. A reasonable interpretation of the cited "a virus" in claim can be any virus in the art as claim 19 drafted.

21. It is well known in the art different families of viruses have different structures and replication machineries (Please see Virus Repication published by Microbiology @ Leicester: Virology: Virus Replication on October 22, 2004, pages 1-20, especially the 2md and 5rd pages). For example, although HIV and HCV are both RNA viruses, they replicate via complete different replication and packaging mechanisms using complete different viral enzymes encoded by different genes (Please see The HIV Life Cycle, published by OpenChemist.Net on June 05, 2006, pages 1-15 and Brass et al. Int. J. Med. 2006, Vol. 3, pages 29-34), such that HIV uses reverse transcriptase encoded by the pol gene to reverser transcribe the viral RNA into proviral DNA followed by translating said proviral DNA into HIV viral RNA, whereas HCV does not need this step. It uses RNA dependent RNA polymerase (RDRP) encoded by the HCV NS5B to complete the HCV viral RNA synthesis. Therefore, one cannot use only GBV-B virus genome or partial HBV-B viral genome to produce any or all virus unless the GBV-B virus replication

replicon comprising other virus's replication control and structural genetic elements. However, the claims are not drafted to comprise any other virus's elements.

22. GB virus B (GBV-B) is the most closely related virus to the hepatitis C virus (HCV) and is an attractive surrogate model system for HCV replication and drug development. Unfortunately, GBV-B can only grow in the primary hapatocytes or certain non-human primates as evidenced by Buckwold et al. (Antiviral Research 2005, Vol. 66, pp. 165-168).

23. It has been noted that Applicants in response assert that the publication by Dr. Buckwood et al. is susceptive, and Dr. Tomassi et al. paper supports that GBV-B virus can replicate in Huh-7 , HepG2 cell. However, applicants are reminded that none of these references at least supports the broad scope of the claims that reads on using any or all host cell being able to replicate a HCV replicon. Up to now the replication of a transfected HCV replicon can only be succeed in tow human hepatoma cell line Huh-7 or hepG2. It suggests that the replication of HCV replicon may depend on distinct cellular factors (See Bartenschlager et al. J. Gene. Viro. 2000, Vol. 81, pp. 1631-1648, especially on page 1638, 1st column, lines 11-13 and page 1639, last paragraph on 2nd column). Therefore, it is still unpredictable that every cell line can be used for support the HCV sub-genomic replicon replication because the state of art teaches although the production of infectious virus from cells transfected with cDNA or RNA.

24. Moreover, while specification teaches several chimeric GBV-B/HCV virus or recombinant GBV-B virus, wherein the chimeric GBV-B/HCV is made by substitution of GBV-B genetic elements with the corresponding genetic structures of a HCV into the background of GBV-B virus replicon; all recombinant GBV or chimeric GBV-B/HCV virus produced contain the full length of 3' terminal nucleotides of SEQ ID NO: 1, and they are able to be reproduced by introducing said recombinant or chimeric virus into the liver of a tamarin. The specification does not provide a sufficient evidence to support the broad scope of the claims that is directed to use said approach for producing any or all viruses. The specification does not teach which 50-100 contiguous nucleotides of SEQ ID NO: 1 or 70% to 95% of SEQ ID NO: 1 or which 250-5000 of SEQ ID NO: 2 are required for producing any or all virus.

25. Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan

would have to conduct undue and excessive experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

26. Claims 51-53 are still rejected under 35 U.S.C. 102(e) as being anticipated by Traboni C. (US patent No. 6,627,437B1) in light of disclosure of NCBI gene bank for NCBI AJ277947 cited by Sbardellati et al. (J Gene. Virol. 2001, Vol. 82, pp. 2437-2448) on the same ground as stated in the previous office action.

27. Applicants' argument regarding to the 102(e) date of the cited reference US patent (US patent No. 6,627,437B1) is correct. The rejection over claims 19-20, 30-33 is withdrawn.

28. However, the benefit for the earlier effective filing date of claims 51-55 in the current application is still denied, since they lacks of enablement disclosure under the first paragraph of 35 U.S.C. 112 as discussed above. The effective filing date of claims 51-55 is still considered to be June 05, 2000, which is the later than the effective filing date of the cited reference (US patent No. 6,627,437B1).

29. To this context, claims 51-53 are still rejected under 35 U.S.C. 102(e) as being anticipated by Traboni C. (US patent No. 6,627,437B1) in light of disclosure of NCBI AJ277947.

30. The disclosure of US patent No. 6,627,437B1 teaches a method of using a polynucleotide or its translated RNA to produce GBV-B recombinant virus in tamarin, wherein the polynucleotide sequence is deposited with NCBI accession number AJ277947 submitted on May 21, 2000. The sequence of AJ277947 comprises at least 1000 contiguous but less than 5000 contiguous nucleotide of SEQ ID NO: 2, which also comprises at least 100 consecutive nucleotide of SEQ ID NO: 1 in contact. The sequence of NCBI AJ277947 is evidenced in light of the disclosure of NCBI gene bank cited by Sbardellati et al. (J. Gene. Virol. 2001, Vol. 82, pp. 2437-2448, see the bottom of column 1 of page 2437 in page 1-5), The cited reference by Sbardellati et al. is not used to anticipate, it is only used for substantiating the position of the nucleotide sequence of NCBI AJ277947.

31. Therefore, the claims 51-53 are still anticipated by the cited reference.

Claim Rejections - 35 USC § 102

32. Claims 51-53 are still rejected under 35 U.S.C. 102(a) as being anticipated by Bukh et al. (Virol. Sept. 1999, Vol. 262, No. 2, pp. 470-478) on the same ground as stated in the previous office action.

33. Applicants traverse the rejection and argue that claims 51-55 are entitled for the benefit of priority date of June 04, 1999. The reference of Bukh et al. cannot be used as prior art because it was published on Sept. 1999. The rejection should be withdrawn.

34. Applicants' argument regarding to the benefice of earlier filing date of claims 51-55 has been respectfully considered; however, it is not found persuasive as discussed above. Because benefit of the earlier filing date of claims 51-55 are not granted, since they lacks of enablement disclosure under the first paragraph of 35 U.S.C. 112. Therefore, the effective filing date of claims 51-55 is June 05, 2000, which is the later than the publication date of the cited reference on September 1999.

35. Upon carefully compared the claimed SEQ ID NO: 2 with the sequence disclosed by Bukh et al. the reference of Bukh et al. still anticipates the claims 51-53. Because Bukh et al. teach a method of producing a GBV-B infectious virus comprising steps of transcribing a GBV-B virus RNA in vitro using T7 promoter from a plasmid DNA encoding a full length cDAN of GBV-B virus, wherein said cDAN (Please see the accession number AF17962 shown on the page 470) that comprises at least 1000 but less than 5000 contiguous sequence of SEQ ID NO: 2 and 100% homology sequence to the claimed SEQ ID NO: 1 at the 3' non-translated region (See pages 476-477). Therefore, the claimed invention is anticipated by the cited reference.

It is noted that claim 29 is current withdrawn from the above rejections because it is in impropriate dependent form. However, when the problem of claim 29 is fixed in the upcoming response, the claim may be still rejected and also make the Final according to which the amended claim 29 is depended by then.

Conclusion

No claims are allowed.

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Baoqun Li

Bao Qun Li / BAOQUN LI, MD
PATENT EXAMINER